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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

TUCKER, ZACHARY C

ART UNIT PAPER NUMBER

1624

DATE MAILED: 03/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/656,567

Applicant(s)

DAUGS, EDWARD D.

Examiner

Zachary C. Tucker

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-41 is/are pending in the application.
- 4a) Of the above claim(s) 40 and 41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 December 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

As requested by applicant's counsel in the correspondence filed 27 December 2005, which was in reply to the amended Requirement for Restriction mailed 22 November 2005, claims 1-21 have been cancelled, claim 22 has been amended and new claims 24-41 have been added.

Requirement for Restriction

Applicant's election of the invention of Group III in the reply filed on 27 December 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

In the reply, applicant's counsel indicates that all of new claims 24-41 are within the scope of the invention of Group III, which was elected for prosecution (page 13 of the reply). Upon review of these newly added claims, however, the examiner would submit that claims 40 and 41, which are drawn to products made by the process of claims 22-39, are *not* within the scope of the invention of Group III. Group III, as set forth in the Requirement for Restriction mailed 22 November 2005, includes only processes for enantioselectively producing phenoxy(phenyl)acetic acid derivative compounds. A search of the prior art for determining the patentability of the process of claims 22-39 will not address the issue of whether or not the products made by such a process are novel and unobvious. Perhaps most importantly in this respect, no claim drawn to the product of claims 22 and/or 23 was previously presented. If there had been, those claims would have been the subject of a separate Group in the Requirement for

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Restriction. Claims 40 and 41 are therefore withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. At least one product of the process of claims 22-39, (-)-halofenate, has in fact been known for a long time, as will be evident from the cited references in this Office action. For at least this reason, claims 40 and 41 are not seen as being patentable, notwithstanding their having been withdrawn from consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 includes the indefinite claim language explained below. Since all of instant claims 23-39 depend either directly or indirectly from claim 22, all claims incorporate indefinite claim language and are therefore included in this rejection.

The terms "the racemic mixture" and "the α -(phenoxy)phenylacetic acid" in step (a) of claim 22 lack antecedent basis within the claim. No previous recitation of any racemic mixture or any phenylacetic acid appears in the claim, yet the phrases "the racemic mixture" and "the α -(phenoxy)phenylacetic acid" necessarily refer back to some earlier recitation thereof. In the examination of claim 22, the claim has been treated with respect to the prior art as if some antecedent basis existed for these two claim elements. The MPEP directs the examiner to apply art against a claim if the degree of uncertainty about the claim's meaning is not great, and where at least one interpretation of that claim would render it unpatentable

over the prior art (2173.06). Art has been applied against the instant claims bearing this in mind.

Claim 24, in addition to being indefinite because it depends from indefinite claim 22, is further indefinite for the recitation of "... sufficient to produce the ratio of the amount of the free first enantiomer to the amount of the free second enantiomer in the solution is about 1 to 3..." When described in the manner noted, the ratio is not clear and well defined. The language could be interpreted as signifying a range of ratio of from about 1:1 to about 1:3 (because the unspecified element of the ratio is assumed to be one in such cases while variable element is the one specified) or only a single ratio of "about 1:3." Since the standard notation of mathematical ratios, numbers separated by a colon, is not employed in instant claim 24, it is not possible to interpret exactly which of the two possibilities applicants intended. Lastly, with respect to instant claim 24, the recitations of "first enantiomer" and "second enantiomer" complicate understanding of the claimed process, because these are not defined with respect to which is desired (the enantiomer being concentrated) and which is not (the enantiomer that is not being concentrated).

Claim 25, in addition to being indefinite because it depends from indefinite claim 22, is further indefinite because steps (i) and (ii) in that claim are not understood. How the solution temperature can be both raised and lowered simultaneously in step (ii), as the claim infers, because no language indicating a sequence of events is recited, is not possible. Furthermore, the phrase "first enantiomer to an enantiomerically enriched α -(phenoxy)phenylacetic acid" presents logical problems in its interpretation. Exactly what constitutes an

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enantiomer to an enantiomerically enriched compound is unknown to the examiner, and is not defined in the specification. In both steps (i) and (ii) of claim 25, reference is made to "a first enantiomer." As explained in the preceding sentences, which enantiomer this first enantiomer is, the one being enriched or the one not being enriched, is not made clear. In order to understand the process being claimed, one of ordinary skill must know which enantiomer is being referred to, the one being enriched or the undesired enantiomer. These two enantiomers have different nucleation temperatures, so which is being referred to is critical for understanding the temperature limitations of step (ii).

Claims 24 and 25 have not been further examined on the merits in this Office action, because to do so would be overly speculative on the part of the examiner. As noted above, if the degree of uncertainty about a claim's meaning is not great, the examiner should apply art against an indefinite claim. In the instant case, the degree of uncertainty is too great. Since claim 26 depends from claim 24, it has not been further examined as well.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22, 23 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by US 6,262,118 (Luskey et al).

Starting at Example 4 of Luskey et al, to Examples 5 and 6, Luskey et al discloses preparation of enantiomerically enriched (-)-halofenate, as specified in instant claims 22 and 23.

The (-) enantiomer of the α -(phenoxy)phenylacetic acid starting material is prepared from the racemic acid in Example 4, by adding a total of about 1 molar equivalent of (-)-cinchonidine. This step of Luskey et al's resolution process meets the limitation of part (a) of instant claim 22 because the claim places *no limitation* on the *total amount* of the enantiomerically enriched chiral amine compound, just that the amount employed must include less than 0.5 molar equivalents, which a total of about 1 molar equivalent does. Indeed, in Example 4 of Luskey et al, less than 0.5 molar equivalents of cinchonidine are used, as well as another portion which represents more than 0.5 equivalents thereof. The (+) isomer of α -(phenoxy)phenylacetic acid precipitates from the solution and is isolated, while the (-) isomer remained in solution and is later finally isolated by addition of sulfuric acid (col. 29, lines 15-27).

Subsequently, in Example 5 of Luskey et al, the purified (-) isomer of α -(phenoxy)phenylacetic acid is reacted with thionyl chloride and converted to the acid chloride derivative. This step meets the limitation of part (b) of instant claim 22 and claim 27. The broadest reasonable interpretation of "recovering" reads on simply separating the chiral amine compound from the α -(phenoxy)phenylacetic acid. Since the product (the enantiomerically enriched acid) is extracted into the organic phase (col. 29, lines 26-27), the chiral amine compound remains in the aqueous phase; it has been recovered.

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Lastly, the acid chloride from Example 5 of Luskey et al is allowed to react with N-acetoethanolamine, to form (-)-halofenate.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Luskey et al.

Luskey et al is applied to instant claims 28-30 as set forth above in the rejection of claims 22, 23 and 27 under 35 U.S.C. 102(b).

At the time the invention was made, the process of claims 28-30 would have been obvious to one of ordinary skill in the art, given the teaching of Luskey et al.

The limitations posed by claims 28-30 are expedients well-known to the chemist of ordinary skill. Reusing a resolving agent, as specified in claim 28 is obvious. The motivation to reuse the resolving agent is to decrease the overall cost of performing the resolution. As applicant can appreciate, chiral amines for resolution of enantiomers have a monetary cost associated with them, and they are unchanged in the salt-formation reaction. Recovering the chiral amine and then introducing it back to the first step of the resolution process is obvious.

Racemization of the undesired enantiomer, in the case of Luskey et al, the (+) enantiomer, by addition of a base, followed by further resolution of the racemized material, is an obvious means for obtaining as much desired enantiomer

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as possible, and decreasing losses. This technique is well-known to the chemist of ordinary skill and the further limitation of racemization of the undesired enantiomer, followed by subjecting that racemized material to further resolution to isolate more of the desired enantiomer, does not represent a patentable distinction over a disclosure of the general resolution process disclosed by Luskey et al, in Examples 4-6.

Abstract of the Disclosure

The examiner wishes to point out that the abstract of the disclosure no longer corresponds to any claimed subject matter; applicant may wish to amend the abstract so as to convey a brief narrative of the invention *claimed*. To do so is not required under 37 CFR 1.72(b), however, since the subject matter described in the abstract in its present form is in fact disclosed in the application.

Allowable Subject Matter

Claims 31-39 would be allowable if rewritten or amended to overcome the rejections under 35 U.S.C. 112, second paragraph, set forth in this Office action. Limitation in claim 31, from which all of 32-39 ultimately depend, of the identity of the chiral amine resolving agent is the patentable distinction of the process of those claims over Luskey et al.

Claims 22, 23 and 27-30 would be allowable if the rejection under 35 U.S.C. 112, second paragraph, were overcome and if claim 22 were amended to explicitly state that the total amount of enantiomerically enriched chiral amine compound was less than 0.5 molar equivalents with respect to the α -(phenoxy)phenylacetic acid compound.

Some enantiomeric resolution processes are known in the prior art (although none involving the α -(phenoxy)phenylacetic acid starting material recited in part (a) of instant claim 22), where a total of half molar equivalent of a chiral amine is employed, resulting in increase optical purity of the product. These procedures require half of a molar equivalent, not less than one half of a molar equivalent of the chiral amine resolving agent, and there would be no motivation to modify these prior art teachings to first of all apply them to the α -(phenoxy)phenylacetic acid of the instant claims, and then to further modify such a process so that less than one half of a molar equivalent of the chiral amine resolving agent is employed, as required by the instant claims. As evidence that nonstoichiometric quantities of resolving agents are known to be employed in enantiomeric resolutions like the one to which the instant claims are drawn, the examiner would cite:

Jean Jacques and André Collet ENANTIOMERS, RACEMATES, and RESOLUTIONS, pages 307-328 © 1981 by John Wiley & Sons, Inc.

Pages 307 and 308 are most relevant. One of the references cited in the bibliography at the end of the cited chapter from Jacques and Collet is:

Read and Reid, "The Complete Optical Resolution of Externally Compensated Acids and Bases" Journal of the Society of the Chemical Industry - London, vol. 47, pages 8T-11T (1928).

This reference is interesting for its report of optical resolutions of racemic tartaric acid with half an equivalent of cinchonine, providing good results. No teaching to employ *less than* half an equivalent of a chiral amine resolving agent is found in Read and Reid, and the phenylacetic acid compounds recited in the instant claims are not the subject of the report.

Also pertinent to the process of the instant claims is GB 1,182,008 (Roberts),

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for its disclosure of a process for making optically pure intermediates for making (-)-halofenate. In Example 2, an enantiomerically enriched α -(phenoxy)phenylacetic acid is produced. No specific reference to preparation of halofenate is made in Roberts, nor any teaching to employ less than one half of a molar equivalent of cinchonidine, the enantiomerically enriched chiral amine compound.

US 3,517,050 and US 3,517,051 (both to William A. Bolhofer) disclose preparation of racemic halofenate; enantiomeric resolution of the isomers is only mentioned in passing (col. 3, lines 54-61).

US 4,214,095 and US 4,786,731 (to Thiele et al and John W. Russell, respectively) disclose compounds of similar structure to those embraced by the structural formula depicted in instant claim 22. The Russell patent teaches enantiomeric resolution of these compounds with D or L alaninol (columns 3 and 4), and the Thiele et al patent mentions that the invention includes both "D" and "L" stereoisomers of the compounds (see abstract).

The instantly claimed process is not seen obvious over nor anticipated over any of the references cited in this section, "Allowable Subject Matter."

Conclusion

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Tuesday-Thursday from 8:00am to 4:30pm or Monday from 6:00am to 1:30pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

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